REMARKS/ARGUMENTS

Claims 1-10 are pending. No amendment is made in the present response. Reconsideration of the present application in view of the following remarks is respectfully requested.

Rejections under 35 U.S.C. §102(a)

In the Office Action, the Examiner first rejects claims 1-10 under) as being anticipated by Lai et al. (Anti-Cancer Drugs, 2003, vol. 14, pages 825-828, accepted for publication on September 3, 2003). As explained in the Rule 132 Declaration enclosed herewith, Lai merely describes the presently named inventors' own invention[1]. The inventors named in the present application, i.e., Yuen-Liang Lai, Yu-Jen Chen, Yu-Fang Hu, and Chi-Liang Kan are the true and only inventors of claims 1-10 of the present application. None of those non-inventor authors, i.e., Hen-Hong Chang, Ming-Jer Huang, Kou-Hwa Cahng, Wen-Hao Su, Hong-Wen Chen, Chang-Hung Chung, We-Yu Wang, and Li-Huan Lin is an inventor of any claim of claims 1-10 of the present application. These non-inventor authors only worked under the direction of the presently named inventors to test the effectiveness and safety of the presently claimed invention. In other words, Lai invention is not by "another" and hence is not prior art to the present application under 35 U.S.C. §102(a). See, e.g., MPEP §706.02(b), §715.01(a), § 715.01(c), and § 716.10.

Therefore, Applicants respectfully request that the Examiner withdraw the rejection of claims 1-10 in view of Lai under 35 U.S.C. §102(a).

Rejections under 35 U.S.C. §103(a)

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ellison et al. (U.S. 2004/0115283) in view of Cheng et al. (J. Intern Med Taiwan 2003; 14:31-36), and Wu (U.S. Patent No. 6,127,688).

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[1] The Declaration is executed by three of the four inventors. We are currently endeavoring to contact Chi-Liang Kan, who no longer is employed with the Assignee.

According to the Examiner, the primary reference Ellison discloses effective treatment of metastatic breast cancer and "metastases from breast. . . cancer", as well as alleviating or reducing symptoms thereof by any mode of administration of arsenic substance to patients. The Examiner also states that Ellison teaches that the arsenic trioxide provides the advantage of sensitization of cancer cells to radiation and/or chemotherapy.

The secondary reference Wu is cited solely to show that principal applications of electron beam radiotherapy are for treatment of skin cancer, head and neck cancer, and breast cancer. Therefore, the Examiner states that a person of ordinary skill in the art would have been sufficiently motivated to topically administer arsenic trioxide that subcutaneous metastatic breast cancer in combination with radiation therapy such as electron beam radiotherapy.

The Examiner cites to the secondary reference Cheng to show that one of ordinary skill in the art would have increased the arsenic concentration/dose to the dose range recited in dependent claim 9 of the present application in the topical or dermal application to treat cutanueous site of cancer, because Cheng teaches that topically applied arsenic lotion is not systemically absorbed.

The Examiner also rejects claims 1-10 under 35 U.S.C. 103(a) as being unpatentable over Ellison in view of Cheng , Medline abstract 95357499, Medline abstract 84139233, and Wu.

The references Ellison, Cheng, and Wu are applied to claims 1-10 on the same basis as applied to claims 1-9 discussed above. The additional two Medline abstract references are cited to show that the radiation dose recited in claim 10 is obvious to a person of ordinary skill in the art.

We respectfully disagree.

As required by MPEP, to establish a prima facie case of obviousness, three basic criteria must be met. (See MPEP 2143 and 706.02 (J), etc.) First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the

reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

None of the three criteria is met in the present 103 rejection.

First, a person of ordinary skill in the art would not have been motivated to modify the method of Ellsion based on the teachings of other prior art, as suggested by the Examiner, to arrive at the present invention. Ellison discloses methods of treating numerous cancerous diseases (see, e.g., paragraphs 0050-00100) in any suitable route of administration such as oral, rectal, vaginal, transdermal, and parenteral (see, e.g., paragraph 0123). However, it provides neither specific example *(in vivo* or *in vitro)* nor other specific direction with respect to topical administration of arsenic composition. Nor does it provide any specific information related to treatment of cutaneuous metastaic cancer. When discussing the possible theory of treatment of using arsenic composition, the inventors, without intention to be limited by any theory, speculate on several mechanisms. Among these speculative mechanisms, the inventors mention that "Finally, arsenic may also act to sensitize the cancer cells to radiation and/or chemotherapy." Nowhere does Ellison specifically suggest that radiation and/or chemotherapy be applied subsequent to the administration of an arsenic composition to cutaneuous metastaic cancer patients, let alone disclosing any benefit or efficacy of such treatment. Therefore, without any specific guidance or teaching, a person of ordinary skill in the art would not be motivated to topically treat cutaneuous metastaic cancer patients with an arsenic composition, followed by radiation therapy. It is particular so considering that pharmaceutical is a highly unpredictable art.

Second, there is no reasonable expectation of successes to modify Ellison based on other references, as suggested by the Examiner. In other words, the combination suggested by the Examiner is "obvious to try" at most. See MPEP 2145X.B. As noted above, Ellison discloses methods of treating numerous cancerous diseases (see, e.g., paragraphs 0050-00100) in any suitable route of administration such as oral, rectal, vaginal, transdermal, and parenteral (see, e.g., paragraph 0123). However, it provides neither specific

example (in vivo or in vitro) nor other specific direction with respect to topical administration of arsenic composition, let alone any feasible dosage. Nor does it provide any specific information (such as in vivo or in vitro example) related to treatment of cutaneuous metastic cancer. It is well-known that pharmaceutical is an unpredictable art. Without any *in vivo* or in *vitro* test, it is difficult to predict whether a certain composition is effective and safe in treating a particular disease. See, e.g., MPEP 2164.03. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Here, as disclosed by Ellison, arsenic is well known to be both a poison and a carcinogenic agent, although there are also many reports concerning the use of arsenic in medial treatment (see paragraph 0022). Therefore, without being advised as to any specific guidance or data, a person of ordinary skill in the art would not have any reasonable expectation of success of treating cutaneous metastaic cancer by topically administering an arsenic composition, followed by transcutaneous application of electron beam to the cutaneuous cancer site.

In other words, even if a person of ordinary skill in the art would try to combine the teachings of Ellison with other references, as suggested by the Examiner, he or she would have to carry out undue experimentation to determine what specific disease can be treated by a specific arsenic composition in a specific manner of administration, etc. Therefore, the combination suggested by the Examiner is merely inadmissible "obvious to try "at most. See MPEP 2145X.B.

The fact that Ellison limits its claims to treatment of only melanoma, despite the broad disclosure in the specification, seems to suggest that the specification does not fairly suggest or teach the treatment of all of the numerous cancerous diseases mentioned in the specification.

Moreover, as explained in paragraph 0030 of the present application, treatment of cutaneuous metstatic cancer with radiation therapy or chemotherapy is disappointing. This would further discourage a person of ordinary skill in the art from applying radiation therapy to a cutaneuous metstatic cancer patient after the treatment with an arsenic composition. In other words, the beneficial results of the combination of the

present invention (see, e.g., paragraphs 0028-0041 of the specification) would have been unexpected to a person of ordinary skill in the art prior to the time the present invention was made.

Third, the references combined by the Examiner to reject, e.g., claim 1, fail to disclose all the limitations cited in the claims. For example, the Examiner admits that the primary reference Ellison does not teach a method of treating cutaneuous metastatic cancer, although Ellison mentions numerous different cancers, such as breast cancer. Nor does the Examiner explicitly remedy this deficiency of Ellison with any other references. Rather, the Examiner simply asserts that it would have been obvious for a person of ordinary skill in the art to treat subcutaneous cancer based on Ellison. The Examiner does not explicitly inform where this missing limitation as to "cutaneuous metastatic cancer" can be found, i.e., is it well-known knowledge, the Examiner's personal knowledge, or disclosed in any other reference? In fact, even if the Examiner had explicitly identified this missing limitation, as discussed above, he would also have to specify why a person of ordinary skill in the art would have combined this missing limitation with the teaching of Ellison to arrive at the present invention with a reasonable expectation of success.

Based on the foregoing, claims 1-10 are not obvious over the cited prior art, individually, or taken together, under 35 U.S.C. § 103(a). Withdrawal of the rejections of claims 1-10 under under 35 U.S.C. § 103 is respectfully requested.

Therefore, Applicants believe that the present application has been placed in condition of allowance. Early and favorable consideration is respectfully requested.

It is believed that no other fees or charges are required at this time in connection with the present application. However, if any fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,
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